Journal of Medical Diagnostic Methods
ISSN: 2168-9784

Namal and Sabet, J Med Diagn Meth 2018, 7:3
DOI: 10.4172/2168-9784.1000276

Research Article Open Access

Diagnostic Accuracy of 3T MR in Staging of Uterine Cervical Carcinoma

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Received date: August 17, 2018; **Accepted date**: September 04, 2018; **Published date**: September 11, 2018

Abstract

Objective: We aimed to evaluate the diagnostic accuracy of 3T MRI sequences for staging of uterine cervical carcinoma (CC).

Methods: We examined 22 cases of CC by a 3T MRI with T2W single shot turbo spin echo, diffusion weighted imaging (DWI) and post-contrast dynamic T1W images. The quantitative evaluation of dynamic series was also performed.

Results: For parametrial invasion, DWI and early phase post-contrast images yielded higher diagnostic accuracy. DWI showed 86% sensitivity, 41% specificity, 80% diagnostic accuracy, 100% PPV, and 70% NPV. Post-contrast early phase images yielded 80% sensitivity, 71% specificity, 77% diagnostic accuracy, 86% PPV, and 62% NPV. T2W sequences showed 73% sensitivity, 71% specificity, 73% diagnostic accuracy, 85% PPV, and 55% NPV. Late phase contrast-contrast images yielded 60% sensitivity, 71% specificity, 64% diagnostic accuracy, 82% PPV, and 45% NPV.

Conclusion: 3T MRI has high diagnostic accuracy in the preoperative staging of CC especially with DWI.

Keywords: Gynaecological oncology; Uterine cervical carcinoma; Parametrial invasion; Staging; Magnetic resonance imaging; Diffusion weighted imaging; Radiologic imaging

Introduction

Uterine cervical cancer (CC) is the third most common gynaecological malignancy following endometrial and ovarian cancers [1]. Since treatment and prognosis are mainly based on histological grade, extent of infiltration (parametrial, pelvic side wall invasion), tumor size, and lymph node involvement, accurate preoperative staging is critical. Presence of parametrial invasion also affects prognosis and management. Patients with parametrial invasion are treated with definitive chemo-radiotherapy. Radical hysterectomy with bilateral pelvic lymph node dissection is the preferred treatment for stage 1 and 2A. Staging of CC is usually performed at clinical examination under anaesthesia and often with cystoscopy, chest radiography, renal ultrasonography (US) and sigmoidoscopy according to the FIGO (International Federation of Gynecology and Obstetrics) classification system [2,3]. However, there were discrepancies seen at clinical staging and surgery as high as 32% in patients with stage 1B disease and 65% in patients with stage 3 disease [4]. The FIGO committee updated the previous staging of 1988 by introduction of the revised staging scale in June 2009 [5]. Now, the revised FIGO staging system recommends magnetic resonance imaging (MRI) as a complementary tool to the clinical assessment.

MRI, thanks to the fine assessment of the anatomy of the cervical wall and the pelvic structures, is actually preferred over US and computed tomography (CT) for local staging of gynaecological malignancies especially in endocervical lesions [2,6]. The usefulness of 1.5 and 3T MRI in the staging of CC has been reported in several studies [7-13]. Previous researches have tended to focus on conventional sequences rather than DWI. An additional problem is that most of them have analysed the ADC values of tumour and compared with those of the normal cervical tissue before [14-18] or after [19-22] chemo radiotherapy. To our knowledge, the potential of DWI in local staging has not been studied with 3T MRI. Our purpose was to evaluate the diagnostic performance of 3T MRI scanner sequences in staging of CCs and to review previous experiences reported in the literature.

Materials and Methods

Subjects

Twenty-six consecutive patients with the diagnosis of stage ≥ 1B CCs established by biopsy were included in this prospective study. Two subjects with lesions less than 1 cm in diameter, due to limited resolution of the DWI and two claustrophobic subjects were excluded. Thus, the final study population comprised 22 patients (mean age 57.7 ± 11.8 years, range 34-75 years) including 15 squamous cell and 7 adenocarcinomas.

Clinical staging, according to FIGO (5) was performed for all the 22 patients through physical examination findings under anesthesia, chest radiography, and renal US. At clinical examination, 7 patients were staged ≤ 2A [stage 1B (n=5), 2A (n=2)] and 15 patients were staged ≥ 2B [stage 2B (n=7), stage 3A (n=2), stage 3B (n=1), stage 4A (n=2), and stage 4B (n=3)]. Radical hysterectomy, salpingoophorectomy and

pelvic lymph node dissection was performed in 7 patients (clinically staged as <2B) within approximately 10-15 days (mean: 12 days) of MRI. The standard of reference for the statistical evaluation was histhopathology. Radiotheraphy was performed for all the remaining 15 patients (clinically staged ≥ 2B). The standard of reference for statistical evaluation was based on clinical FIGO staging system [5] in these patients.

Following approval of the institutional review board and protocol review committee, consent was waived from all subjects to use their clinical data for educational and research purposes, with the patient privacy secured.

MR examination

All images were obtained with a 3T scanner (Philips Achievea Intera Release, Eindhoven, The Netherlands). The coil type was 16-element phased-array body coil. All imaging examinations were performed following a 6 hour fasting period to limit artifacts of small bowel peristaltism. Detailed imaging protocol and parameters are mentioned in Table 1. Initially, unenhanced axial T1 Weighted (W) THRIVE (T1 High Resolution Isotropic Volume Examination) and axial T2W images with fat suppression were obtained to evaluate the pelvic lymph nodes. Three-plane axial, sagittal, and coronal oblique (parallel to the short and longitudinal axis of the cervix) small field of view (FOV) (21-24 cm) T2W without fat suppression was employed for detection of the main cervical lesion and its extension. Afterwards, four series of axial oblique DWI were acquired and apparent diffusion coefficient (ADC) maps were generated from b0 and b1000 sec/mm² images. Gadopentate dimeglumine (Gd-DTPA) (Magnevist®, Schering, Germany) was used as contrast agent in this study with dose of 0.1 mmol/kg. Dynamic imaging was performed following intravenous administration of the contrast agent into antecubital vein with 5 ml/s. The same precontrast parameters for T1W THRIVE was applied in dynamic images obtaining nine dynamic series with 20 seconds intervals between 0^{th} and 180^{th} seconds. Afterwards, an additional late phase postcontrast T1W THRIVE image at 5^{th} minute was obtained. The fat suppression technique was SPAIR (Spectral Adiabatic Inversion Recovery). Shortening of imaging time and prevention of probable susceptibility artifacts was provided by application of partially-parallel imaging acquisition called SENSE reconstruction with a reduction factor of 2 in all sequences. Dielectric pad was not used. Total acquisition time was 20-25 minutes.

Parameters	Precontrast THRIVE	SSh-TSE T2 FS	SSh-TSE T2 Without FS	Postcontrast THRIVE	DWI
Plane	Axial	Axial	Axial	Axial, Sagittal, Coronal oblique	Axial oblique
Repition Time (ms)	500	1000	1000	500	2000
Echo Time (ms)	20	80	80	20	671
NEX	2	2	2	2	1
Flip Angle (°)	10°	15	15	10°	-
Field of view (cm)	21-24	21-24	21-24	21-24	21-24
Fat Supression	SPAIR	SPAIR	-	SPAIR	-
Slice Thickness (mm)	0,6	4	4	0,6	4
Intersection Gap (mm)	0	1	1	0	1
Matrix Size (Pixel)	125 x 125	112 x 125	112 x 125	125 x 125	112 x 125
EPI Factor	-	-	-	-	45
b value (sec/mm²)	-	-	-	-	0, 1000
Sensitizing Gradient Direction	-	-	-	-	x, y, z
SS-TSE: Single Shot-Turbo Spin Echo; FS: Fat Saturation; DWI: Diffusion Weighted Imaging; SPAIR: Spectral Adiabatic Inversion Recovery					

Table 1: Imaging parameters for MRI examination.

Image analysis

One radiologist (S.S), who was unaware of the results of the clinical staging and histopathological results, performed quantitative measurements on a dedicated workstation (Philips MR workspace, Release 2.5.3.0; The Netherlands).

Diagnostic value of the sequences

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy for parametrial involvement were analysed for DWI, T2-W, early (20^{th} sec), and late (5^{th} min) phase postcontrast images separately. Parametrial invasion was defined as a disruption of the hypointense line circumscribing the cervix on oblique T2W images, tumor presence in the parametrium, a spiculated tumor-parametrial interface, tumor encasement of periuterine vessels, or existence of hydronephrosis [23]. Concerning the parametrial infiltration, stages 1B and 2A were considered negative, while stages 2B, 3 and 4 were considered positive.

Quantitative evaluation of post-contrast series

Wash-in rate (WIR), maximum relative enhancement (MRE), and time-to-peak enhancement (TTP) values of the lesions were determined from SI-time curves on a dedicated workstation.

Quantitative evaluation of DWI

The measurement of signal intensities (SIs) of the normal cervical tissue and carcinomas was performed on b factor of 1000 sec/mm² DW trace image with a region of interest (ROI). ADC maps were generated from 0 and 1000 sec/mm² images. After determination of ADC values of the carcinomas and normal cervical tissue from three different foci, the average of these three measurements was considered as the final ADC value for both tumor area and normal tissue.

All of the ROIs were placed manually over the tumor foci and normal cervical tissue based on the T2 W morphological information. On DWI and ADC map, ROIs placed in identical locations on axial T2 W images. For the tumor foci, a ROI was drawn at the center of the tumor. ROI was set to a possible maximum size to prevent interference from the surrounding normal tissue.

Statistical analysis

Sensitivity, specificity, PPV, NPV, and diagnostic accuracy of T2W, DWI, post-contrast early (20th), and late phase (5th min) images were calculated for diagnosis of parametrial invasion. MRE, WIR, and TTP values were compared for quantitative analysis of the dynamic images. The SIs and ADC values of both normal cervical tissue and carcinomas were compared for quantitative evaluation of DWI. Kolmogorov-Smirnov test was used to asses normality of numeric data. Subsequently the differences in these values were analyzed by Student's t test. A p value of >0.05 was considered significant. All statistical analyses were performed using SPSS (Statistical Package for Social Sciences) statistical software.

Results

Analysis of diagnostic performance of acquired sequences

Detailed results concerning the diagnostic performance of the acquired sequences are shown in Table 2. Regarding the parameterial invasion, the diagnostic accuracy of the T2W sequence (Figure 1a) was 73%. Eleven cases were true positive and 4 cases were false negative. The diagnostic accuracy of DWI (Figure 1b and 2a) was 86%. Twelve cases were true positive and 3 cases were false negative. The diagnostic accuracy of early phase T1W sequence was 77%. Twelve cases were true positive and 5 cases were false negative. The diagnostic accuracy of late phase T1W (Figure 1d) sequence was 64%. Nine cases were true positive and 6 cases were false negative.

Quantitative analysis of dynamic images

Normal cervical tissue had significantly higher MRE ($p<0.005$) than cervical carcinomas. The mean MRE for cervical carcinoma and normal cervical tissue were 81.27 ± 39.21 and 140.27 ± 29.06, respectively. There was no statistically significant difference for WIR and TTP values.

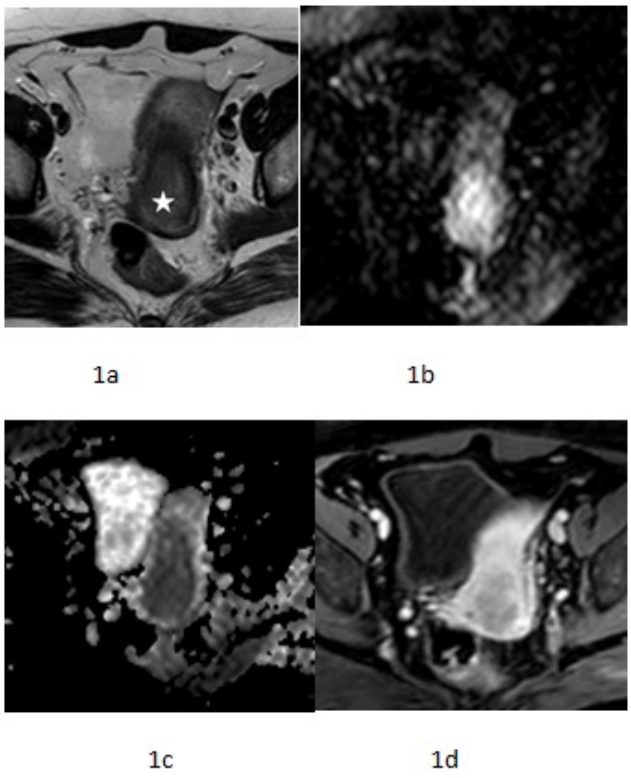

Figure 1: Axial T2W (a) Diffusion weighted trace (b) ADC map (c) Postcontrast T1W (d) Images show a mass in a 43-year-old woman with stage 2a squamous cell carcinoma. The mass is slightly hyperintense on axial T2W image (white star) (a) Remarkably hyperintens on diffusion weighted trace image (b=1000 sec/mm^2) (b) Prominently hypointense on ADC map (ADC value of carcinoma is 0.82 x 10^{-3} mm^2/sec). The normal cervical stroma is seen as a hyperintense wall (c) This mass is seen as an irregular hypovascular area on the postcontrast T1W THRIVE image (d).

The mean WIR for cervical carcinoma and normal cervical tissue were 24.91 ± 14.00 and 25.91 ± 15.31, respectively (p=0.86). The mean TTP for cervical carcinoma and normal cervical tissue were 142.48 ± 54.33 and 147.74 ± 36.73, respectively (p=0.78).

Quantitative analysis of DWI

With b factors of 1000 sec/mm^2, carcinomas had significantly higher SIs than cervical tissue (p=0.02) (Figure 1b and 2a). The mean SIs for carcinoma and normal cervical tissue were 365 ± 153 and 219 ± 110, respectively. Carcinomas had significantly lower ADC values compared to normal cervical tissue (p=0.006) (Figure 1c and 2b). The mean ADCs for cervical carcinoma and normal cervical tissue were 0.87 ± 0.19 x 10^{-3} and 1.25 ± 0.48 x 10^{-3} mm^2/sec, respectively. We analysed the differences of ADCs between different pathologic types but there was not any statistically significant differences.

Parameters	Sensitivity %	Specificity %	Positive predictive value (PPV) %	Negative predictive value (PPV) %
T2-W SSh TSE	73	71	85	55
Early phase (25th sec) postcontrast T1-W THRIVE SPAIR	80	71	86	62
Late phase (5th min) postcontrast T1-W THRIVE SPAIR	60	71	82	45
DWI	80	41	100	70

Table 2: Results of the diagnostic performance of sequences. Note-T2-W SSh TSE (T2 Weighted Single Shot Turbo Spin Echo), T1-W THRIVE SPAIR (T1 Weighted High Resolution Isotropic Volume Examination Spectral Adiabatic Inversion Recovery), DWI: Diffusion Weighted Imaging.

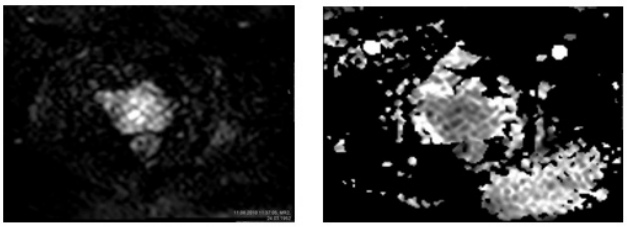

Figure 2: Axial diffusion weighted trace image (a) and ADC map (b) show a mass in a 59 year old woman with stage 2b adenocarcinoma. There is remarkable hyperintensity in the tumor and area of the parametrial infiltration on diffusion weighted trace image (b=1000 sec/mm^2) (a). The tumor and the area of parametrial invasion show a prominent hypointensity on ADC map (b). ADC value of carcinoma is 0.89 × 10^{-3} mm^2/sec.

Discussion

3T MRI systems are being increasingly used in clinical settings. Theoretically, the major advantage of 3T systems should be the higher signal-to-noise ratio (SNR) which translates into higher temporal and spatial resolution [8]. There are only a few reports on the role of conventional T2W sequences obtained with 3T imaging of the CC [7,8]. In contrast to the fibromuscular stroma, CC is seen slightly hyperintense on T2W images. At 3T imaging, mean tumor SNR, mean cervical stroma SNR, and mean tumor-to-cervical stroma contrast-to-noise ratios (CNR) at 3T imaging were significantly higher than those at 1.5T MRI system. Nevertheless, image homogeneity at 3T imaging seems inferior to that at 1.5T imaging. Even if imaging quality seems to be higher at 3T, the diagnostic accuracy was equivalent at 1.5 and 3T systems. Although T2W images play an important role in staging, contrast enhanced dynamic MRI could be useful.

According to current guidelines of the European Society of Urogenital Radiology (ESUR), I.V. contrast is rarely necessary for staging of CC [1]. Hricak et al. [24] found that the assesment of tumor location and size did not improve following contrast enhancement. However, the use of contrast improved the evaluation of disease extent only in stage 2 and higher disease. Van Vierzen et al. [25] evaluated the usefulness of pre-contrast *vs.* post-contrast and fast dynamic MRI in the preoperative staging of CCs. They found that the combination of pre-contrast and post-contrast MRI did not clearly improve staging accuracy (83%). However, the addition of fast dynamic contrast enhanced MRI improved staging accuracy upto 91%. In this study, fast dynamic MR imaging were obtained every 3 sec for 45 s. According to their study, contrast enhancement of the tumor is lower than the myometrium in the early phase. Thus, interpretation of images is easier on the earlier phases of contrast enhancement. The use of contrast enhanced images also improves the accuracy of assessment of bladder and rectal wall invasion. Consistently, cervical stroma showed significantly higher enhancement than those of the carcinomas in our study. Our results of quantitative analysis showed a significant improvement in tumor versus normal cervical tissues on post-contrast images. This feature could be used for evaluating parametrial invasion. As the MRE of cervical tissue significantly higher than those of the carcinoma, the contrast between the cervical tissue and carcinoma more prominent on post-contrast early phase images. In our study, contrast enhanced early phase images showed more diagnostic accuracy than previous studies which were obtained by 1.5T systems. This result may be related to the higer T strength in our study. Theoretically, contrast enhancement effect of gadolinium agents is higher at 3T because longer relaxation times yield a stronger T1 reduction.

DWI is becoming an important noninvasive technique for characterization of lesions. Although there is few published data, DWI seems to be a very promising emerging technique in the evaluation of CC. In most of them, the ADC values of tumor were analysed and compared with those of the normal cervical tissue at before [14-18] or after [19-22] chemoradiotherapy. In all of them, malignant masses showed lower ADC value than normal cervical tissue because of higher cellular content. Liu et al. [15] and Kuang et al. [16] also reported that the ADC value of CC correlated negatively with celllular density and the grading of tumor. In addition, Chen et al. [17] evaluated the clinical value of whole-body DWI (WB-DWI) in the staging of uterine CC. They reported that, WB-DWI scan is useful for distinguishing metastatic nodes from benign nodes. In a study with 3T system, mean ADC of CC and normal cervical tissue were reported as 0.97 ± 0.18 x 10^{-3} and 1.62 ± 0.23 x 10^{-3} mm^2/sec, respectively [18]. In our study, the mean ADC values of carcinoma were significantly lower than those of the normal cervical tissue in agreement with the results obtained by previous studies (the mean ADCs for cervical carcinoma and normal cervical tissue were 0.87 ± 0.19 x 10^{-3} and 1.25 ± 0.48 x 10^{-3} mm^2/sec, respectively). This result suggest that ADC measurement has a potential ability to differentiate between the normal and cancerous tissue. Although there are several reports about the known role of DWI in identifying cancer lesions, to our knowledge, there is no reported study on DWI while other studies have utilized DWI as an ancillary technique to T2W. The potential of tumor staging with high b value

DWI was proved in our study, the advantages of higher SNR and better image contrast at 3T. Our study show that parametrial invasion can be evaluated on trace images in which CCs can be clearly depicted as an hyperintense area compared with the suppressed normal cervical tissue. Theoretically, the major advantage of 3T systems should be the higher SNR which translates into higher temporal and spatial resolution on T2 and T1 W images, as well as DWI. However, susceptibility artifacts increase with field strength causing significant geometric image distortion, stretching, and blurring on DWI, particularly in areas of pelvis adjacent to gas-filled loops of bowel [26]. In our study, DWI was acquired using a partially-parallel imaging acquisition (SENSE reconstruction with a reduction factor of 2 to speed up images acquisition and to prevent susceptibility artifacts. Recent studies [27,28] and a meta-analysis [29] have outlined good performance of 3T MRI in diagnosis of parametrial invasion.

Our study had a number of limitations. First, this is limited by the relatively small number of patients. Further studies on larger series are needed to evaluate the diagnostic performance of 3T sequences. Second limitation is that, most of the women were staged only at clinical examination and clinical FIGO stage was considered as standard of reference for the statistical evaluation in these patients. Clinical findings were highly suggestive or clearly indicative of parametrial invasion, however this could have been misleading. Third, our routine pelvic imaging protocol did not include any upper abdomen sequences. Because of that reason, lymph node metastases were evaluated at only pelvic area on large FOV images. Therefore our results for the diagnosis of lymph node metastases may be somewhat inaccuarate.

Indeed, currently no clinical or imaging (MRI,CT,PET scan) examination is capable of exact definition micrometastases of lymph nodes. Compared with radiologic methods, surgical staging is more accurate for assessment of paraaortic nodal disease. However, surgical staging has produced only a modest boost in survival rates, because of the high rate of pelvic and systemic failure [30,31].

In conclusion, 3T MRI allows high resolution images without prominent artifacts. 3T MRI has high diagnostic accuracy in the preoperative staging of patients with cervical cancer especially with DWI.

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